REMARKS

Applicants request reconsideration of the above-identified application in view of the foregoing amendments and following remarks.

The Claim Amendments

In response to the pending rejections, applicants have amended claims 1, 24 and 28 to recite a Syrian hamster prion protein gene promoter. Support for this amendment can be found, for example, on page 4, lines 6-11, of the specification. These amendments merely clarify the claims and are not narrowing amendments.

Applicants have also amended claims 3, 38 and 39 to recite a "C3H x C57 mouse" and claim 7 to recite "mouse".

Applicants have cancelled claims 8-23 and 29-35 as they are drawn to a non-elected invention. They have also cancelled claim 27 without prejudice.

None of the amendments are new matter.

Therefore, claims 1, 3, 5-7, 24, 28 and 38-39 are now pending in this application.

The above amendments are made specifically without waiver of applicants' rights to continue to prosecute and to

obtain claims directed to the deleted subject matter in other applications claiming benefit herefrom.

The Objection

Improper Dependent Form

Claims 38 and 39 are objected to under 37 CFR 1.75(c), for allegedly failing to further limit the subject matter of a previous claim. The Examiner states that claims 38 and 39, which depend on claims 1 and 24 respectively, redundantly limit the mouse's genetic background.

Applicants traverse. Applicants submit that C57BL mice are a strain of C57 mice. Thus, claims 38 and 39 further limit claims 1 and 24, respectively.

Applicants respectfully request that the Examiner withdraw the rejection.

The Rejections

35 U.S.C. § 112, First Paragraph: Written Description

Claims 1, 3, 5-7, 24, 28, 38 and 39 are newly rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the written description requirement. The Examiner states that while the claims are drawn to use of a cos.Tet promoter, nothing in the art or specification

provides any guidance as to what a cos.Tet promoter is. According to the Examiner, the specification refers to a cos.Tet expression construct but that the expression construct is not a promoter.

The Examiner further states that, while the specification refers to a cos.Tet expression construct, it does not provide guidance to the structure of the cos.Tet promoter so that one of skill in the art could obtain such promoters. Thus, the Examiner states, cos.Tet promoters do not meet the written description provision of 35 U.S.C. § 112, first paragraph.

Applicants have amended claims 1, 24 and 28 to recite a Syrian hamster prion protein gene promoter to facilitate prosecution. The specification teaches, inter alia, the use of a Syrian hamster prion protein gene promoter to yield transgenic mice which exhibit multiple diffuse amyloid deposits (see page 4, lines 12-16) and the use of such a promoter for generating TgCRND8 Transgenic Mice (see Example 1 citing Scott, et al., *Cell*, 1989, 59:847-857). Thus, the specification, as filed, satisfies the 35 U.S.C. § 112, first paragraph, written description requirement for the Syrian hamster prion protein gene promoter. Applicants respectfully request that the Examiner withdraw the outstanding rejection.

35 U.S.C. § 112, First Paragraph: Enablement

Claims 1, 3, 5-7, 24, 28, 38 and 39 remain rejected in modified form under 35 U.S.C. 112, first paragraph, for allegedly failing to comply with the enablement requirement. The Examiner states that while the specification is enabling for the claimed "... C3H x C57 mouse whose genome comprises a transgene comprising a nucleotide sequence operably linked to a Syrian hamster prion protein gene promoter..." and the claimed method for producing such a mouse, that it is not enabling for "... a C3H x C57 mouse whose genome comprises a transgene comprising a nucleotide sequence operably linked to a cos.tet promoter..." nor a method for producing such a mouse. The Examiner states that the claims are drawn to the use of a cos.Tet promoter, but that nothing in the specification or the art teaches what a cos.Tet promoter is.

As stated above, applicants have amended claims 1, 24 and 28 to recite a Syrian hamster prion protein gene promoter. The Examiner has acknowledged that the use of a such a promoter is enabled by the specification (see pages 7-8 of the Office Action). Accordingly, applicants respectfully request that the Examiner withdraw the rejection.

The Examiner has also rejected claim 7 and states that claim 7, drawn to a mouse which has a C3H x C57 mouse as

its ancestor, embraces descendent mice which have an FVB/N genetic background. The Examiner further states that the specification teaches that such mice are prone to premature death in early adult life and that the specification does not provide guidance as to how to use mice with this genetic background.

Applicants traverse. The Examiner alleges that the mice of claim 7 are prone to premature death and that the specification does not provide guidance on how to use such a mouse. The specification in fact teaches that "[a]lthough mice containing the FVB/N genetic background are prone to premature death in early adult life...this tendency is attenuated in a genetic background derived from C57 and C3H strains. The TgCRND8 mice therefore establish that levels of Aß peptide can be tolerated without compromising viability" (emphasis added; see Example 1). As the mice of claim 7 have a genetic background derived from C57 and C3H strains (they have C3H x C57 mice as ancestors), one of skill in the art would recognize that their viability would not be compromised.

Further, applicants describe studies on the offspring of TgCRND8 mice (C57 X C3H genetic background) wherein neuropathological changes, behavioral changes and changes in mouse phenotype are observed (see Examples 2-4).

Accordingly, the skilled artisan, equipped with the instant specification and standard techniques in the art, would be enabled to make and use the mice of claim 7. Thus, applicants respectfully request that the Examiner withdraw the rejection.

The Examiner has also rejected claim 24 and states that "the specification does not provide guidance on how to obtain a cos.Tet promoter...and mice of any genetic background and the claims are thus rejected for use of this promoter and any genetic background."

Applicants have amended claim 24 to recite a Syrian hamster prion protein gene promoter thus overcoming the Examiner's rejection.

In light of the above comments and amendments, applicants respectfully request that the Examiner withdraw all pending 35 U.S.C. § 112, first paragraph, enablement rejections.

35 U.S.C. § 112, Second Paragraph: Indefiniteness

Claims 3, 7, 38 and 39 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicants regard as their invention. The Examiner states that there is

insufficient antecedent basis in claim 1 for the limitation of "transgenic mouse" in claims 3, 7 and 38. The Examiner also states that there is insufficient antecedent basis for the "transgenic mouse" of claim 39 in claim 24.

Applicants traverse. However, solely to expedite prosecution, applicants have amended claims 3 and 38 to recite "[t]he C3H x C57 mouse of claim 1"; claim 7 to recite "[a] mouse having the C3H x C57 mouse of claim 1 as an ancestor"; and claim 39 to recite "[t]he C3H x C57 mouse of claim 24" thus obviating the Examiner's rejection.

In light of the above amendments, applicants respectfully request that the Examiner withdraw the outstanding 35 U.S.C. § 112, second paragraph, rejection.

35 U.S.C. § 102

Claim 27 stands rejected under 35 U.S.C. § 102 Claim as allegedly being anticipated by Hsia et al., 1999, PNAS, 96:3228-3233 ("Hsia"), as evidenced by Jin et al., 2004, PNAS, 101:13363-13367 ("Jin"), and Selkoe, 2002, Science, 298:789-791, ("Selkoe"). The Examiner states that Hsia anticipates claim 27, drawn to a nucleotide sequence encoding human amyloid precursor protein 695, wherein the lysine residue at position 670 is substituted by asparagine, the methionine

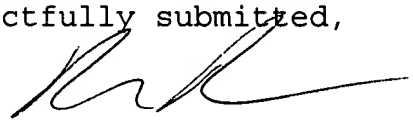
residue at 671 is substituted by leucine and the valine residue at position 717 is substituted by phenylalanine, as Hsia teaches a PDGF-$APP_{Sw,Ind}$ construct and that $APP_{Sw,Ind}$ comprise the required mutations.

Applicants traverse. However, solely to expedite prosecution, applicants have cancelled claim 27 without prejudice. Thus, the rejection is moot.

CONCLUSION

For all of the above reasons, applicants request that the Examiner reconsider and withdraw the outstanding objections and rejections, enter the amendments, and pass the resulting claims to allowance.

Respectfully submitted,



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